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AMENDMENT AFTER FINAL
EXPEDITED PROCEDURE
ART UNIT 1632
U.S.S.N. 09/750,779
12013/55202

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AMENDMENTS TO THE CLAIMS:

OFFICE OF PETITIONS

1. (Currently Amended) An implantable medical device comprising a coating on at least a portion thereof ~~of at least one surface~~, said coating comprising:
 - an inner layer of a cationic polyelectrolyte carrier; and
 - a layer of at least one negatively charged therapeutic agent adsorbed onto said inner layer of cationic polyelectrolyte carrier; and
 - an additional layer or layers of cationic polyelectrolyte carrier and an additional layer or layers of at least one negatively charged therapeutic agent adsorbed onto said additional layer or layers of cationic polyelectrolyte carrier, wherein said additional layer or layers of polyelectrolyte carrier and said additional layer or layers of at least one negatively charged therapeutic agent alternate.
2. (Original) The medical device of claim 1, further comprising an outermost layer of a cationic polyelectrolyte carrier which is the same or different from the inner or additional layer or layers of cationic polyelectrolyte carrier.
3. (Currently Amended) The medical device of claim 2, wherein the outermost layer of cationic polyelectrolyte carrier is more hydrophobic and/or more cationic than at least one of the inner or additional layer or layers of polyelectrolyte carrier.
4. (Currently Amended) The medical device of claim 1, wherein at least one of the inner or additional layer of cationic polyelectrolyte carrier comprises human serum albumin, gelatin, chitosan, or a combination thereof.

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5. (Original) The medical device of claim 1, wherein the medical device comprises a stent, a catheter, a balloon catheter, or a combination thereof.

6. (Cancelled).

⁶
7. (Currently Amended) The medical device of claim 1, wherein the at least one of the one or ~~more negatively charged~~ therapeutic agent comprises rapamycin.

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8. (Currently Amended) The medical device of claim 1, wherein the at least one of the one or ~~more negatively charged~~ therapeutic agent comprises paclitaxel.

9. (Cancelled)

10. (Currently Amended) A method of adsorbing at least one negatively charged therapeutic agent onto ~~the surface of~~ a medical device comprising:

(a) coating at least a one portion of ~~at least one surface of~~ a medical device with a cationic polyelectrolyte carrier to form an inner layer of cationic polyelectrolyte carrier;

(b) washing the inner layer of cationic polyelectrolyte carrier with a washing solution;

(c) adsorbing at least one ~~one or more~~ negatively charged therapeutic agents onto the inner layer of cationic polyelectrolyte carrier to form a layer of at least one negatively charged therapeutic agent; and optionally

(d) washing the layer of at least one negatively charged therapeutic agent with a washing solution and repeating steps (a) through (c) one or more times to form multiple layers of cationic polyelectrolyte carrier and at least one negatively charged therapeutic agent until a desired amount of at least one negatively charged therapeutic agent has been adsorbed onto the medical device.

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11. (Currently Amended) The method of claim 10, further comprising the step of coating the outermost layer of the at least one negatively charged therapeutic agent with an outermost layer of a cationic polyelectrolyte carrier which is the same or different from the inner layer or multiple layers of cationic polyelectrolyte carrier.

12. (Original) The method of claim 11, wherein the outermost layer of cationic polyelectrolyte carrier is more hydrophobic and/or more cationic than at least one of the inner layer or multiple layers of polyelectrolyte carrier.

13. (Original) The method of claim 10, wherein at least one of the inner layer or multiple layers of cationic polyelectrolyte carrier comprises a human serum albumin, gelatin, chitosan, or a combination thereof.

14. (Original) The method of claim 10, wherein the medical device comprises a stent, a catheter, a balloon catheter, or a combination thereof.

15. (Cancelled).

¹³
16. (Currently Amended) The method [medical device] of claim 10, wherein the at least one of ~~the one or more~~ negatively charged therapeutic agent comprises rapamycin.

¹⁴
17. (Currently Amended) The method [medical device] of claim 10, wherein the at least one of ~~the one or more~~ negatively charged therapeutic agent comprises paclitaxel.

18. (Cancelled)

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19. (Currently Amended) A medical device comprising at least one negatively charged therapeutic agent adsorbed on at least a portion ~~the surface~~ thereof and produced by a process comprising:

- (a) coating at least ~~a one~~ portion of ~~at least one surface~~ a medical device with a cationic polyelectrolyte carrier to form an inner layer of cationic polyelectrolyte carrier;
- (b) washing the inner layer of cationic polyelectrolyte carrier with a washing solution;
- (c) adsorbing at least one ~~or more~~ negatively charged therapeutic agent onto the inner layer of cationic polyelectrolyte carrier to form a layer of at least one negatively charged therapeutic agent; and optionally
- (d) washing the layer of at least one negatively charged therapeutic agent with a washing solution and repeating steps (a) through (c) one or more times to form multiple layers of cationic polyelectrolyte carrier and at least one negatively charged therapeutic agent until a desired amount of at least one negatively charged therapeutic agent has been adsorbed onto the medical device.

20. (Currently Amended) The medical device of claim 19, wherein the process further comprises the step of coating the outermost layer of the at least one negatively charged therapeutic agent with an outermost layer of a cationic polyelectrolyte carrier which is the same or different from the inner layer or multiple layers of cationic polyelectrolyte carrier.

21. (Original) The method of claim 20, wherein the outermost layer of cationic polyelectrolyte carrier is more hydrophobic and/or more cationic than at least one of the inner layer or multiple layers of cationic polyelectrolyte carrier.

22. (Original) The medical device of claim 19, wherein at least one of the inner layer or multiple layers of cationic polyelectrolyte carrier comprises human serum albumin, gelatin, chitosan, or a combination thereof.

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23. (Original) The medical device of claim 19, wherein the medical device comprises a stent, a catheter, a balloon catheter, or a combination thereof.

24. (Cancelled)

²⁰ 25. (Currently Amended) The medical device of claim ¹⁵ 19, wherein the at least one of the one or ~~more~~ negatively charged therapeutic agent comprises rapamycin.

²¹ 26. (Currently Amended) The medical device of claim ¹⁵ 19, wherein the at least one of the one or ~~more~~ negatively charged therapeutic agent comprises paclitaxel.

27. (Cancelled)

28. (Currently Amended) A method of delivering a therapeutic agent to a target location by implanting in the target location a medical device comprising at least one negatively charged therapeutic agent adsorbed on at least a portion ~~the surface~~ thereof; wherein the medical device is produced by a process comprising:

- (a) coating at least a one portion of ~~at least one surface~~ a medical device with a cationic polyelectrolyte carrier to form a layer of cationic polyelectrolyte carrier;
- (b) washing the layer of cationic polyelectrolyte carrier with a washing solution;
- (c) adsorbing at least one ~~one or more~~ negatively charged therapeutic agent onto the layer of cationic polyelectrolyte carrier to form a layer of at least one negatively charged therapeutic agent; and optionally
- (d) washing the layer of at least one negatively charged therapeutic agent with a washing solution and repeating steps (a) through (c) one or more times to form multiple layers of

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cationic polyelectrolyte carrier and therapeutic agent until a desired amount of at least one negatively charged therapeutic agent has been adsorbed onto the medical device.

29. (Currently Amended) The method of claim 28, further comprising the step of coating the outermost layer of the at least one negatively charged therapeutic agent with an outermost layer of a cationic polyelectrolyte carrier which is the same or different from the inner layer or multiple layers of cationic polyelectrolyte carrier.

30. (Original) The method of claim 29, wherein the outermost layer of cationic polyelectrolyte carrier is more hydrophobic and/or more cationic than ~~at least one of~~ the inner layer or multiple layers of cationic polyelectrolyte carrier.

31. (Original) The method of claim 28, wherein ~~at least one~~ of the inner layer or multiple layers of cationic polyelectrolyte carrier comprises human serum albumin, gelatin, chitosan, or a combination thereof.

32. (Original) The method of claim 28, wherein the medical device comprises a stent, a catheter, a balloon catheter, or a combination thereof.

33. (Cancelled)

²⁷ 34. (Currently Amended) The method of claim ²² 28, wherein the at least one ~~of the one or more~~ negatively charged therapeutic agent comprises rapamycin.

²⁸ 35. (Currently Amended) The method of claim ²² 28, wherein the at least one negatively charged ~~of the one or more~~ therapeutic agent comprises paclitaxel.

36. (Cancelled)

37. (Previously Amended) The method of claim 28, wherein the target location comprises at least one location selected from the group consisting of brain, heart, liver, skeletal muscle, smooth muscle, kidney, bladder, intestines, stomach, pancreas, ovary, prostate, cartilage, bone, lung, blood vessel, ureter, urethra, and testes.

38. (Currently Amended) A method for treating the occurrence or severity of a clinical disease or condition, comprising:

(a) preparing a medical device by:

- (i) coating at least one a portion of at least one surface a medical device with a cationic polyelectrolyte carrier to form a layer of cationic polyelectrolyte carrier;
- (ii) washing the layer of cationic polyelectrolyte carrier with a washing solution;
- (iii) adsorbing at least one ~~one or more~~ negatively charged therapeutic agent effective to treat or reduce the occurrence of the clinical disease or condition onto the layer of cationic polyelectrolyte carrier to form a layer of at least one negatively charged therapeutic agent; and optionally
- (iv) washing the layer of at least one negatively charged therapeutic agent with a washing solution and repeating steps (i) through (iii) one or more times to form multiple layers of cationic polyelectrolyte carrier and at least one negatively charged therapeutic agent until a desired amount of at least one negatively charged therapeutic agent has been adsorbed onto the medical device.

(b) implanting the medical device into a target location in a mammal from which the at least one negatively charged therapeutic agent can treat or reduce the occurrence or severity of the clinical disease or condition.

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39. (Currently Amended) The method of claim 38, further comprising the step of coating the outermost layer of at least one negatively charged therapeutic agent with an outermost layer of cationic polyelectrolyte carrier which is the same or different from the inner layer or multiple layers of cationic polyelectrolyte carrier.

40. (Original) The method of claim 39, wherein the outermost layer of cationic polyelectrolyte carrier is more hydrophobic and/or more cationic than at least one of the inner layer or multiple layers of cationic polyelectrolyte carrier.

41. (Original) The method of claim 38, wherein at least one of the inner layer or multiple layers of cationic polyelectrolyte carrier comprises human serum albumin, gelatin, chitosan, or a combination thereof.

42. (Original) The method of claim 38, wherein the medical device comprises a stent, a catheter, a balloon catheter, or a combination thereof.

43. (Cancelled)

44. (Currently Amended) The method of claim 38, wherein the clinical disease or condition comprises restenosis or angiogenesis and the at least one of the one or more negatively charged therapeutic agent comprises rapamycin.

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~~45.~~ (Currently Amended) The method of claim ³⁰~~38~~, wherein the clinical disease or condition comprises a malignancy or malignant cell growth and the at least one of the one or more negatively charged therapeutic agent comprises paclitaxel.

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³⁷
46. (Previously Amended) The method of claim ³⁰38, wherein the target location comprises at least one location selected from the group consisting of brain, heart, liver, skeletal muscle, smooth muscle, kidney, bladder, intestines, stomach, pancreas, ovary, prostate, cartilage, bone, lung, blood vessel, ureter, urethra, and testes.

47. (Currently Amended) The medical device of claim 1 wherein the at least one of the one or more negatively charged therapeutic agents is selected from the group consisting of: anti-thrombogenic proteins, antioxidant compounds, angiogenic proteins, agents which blocks smooth muscle cell proliferation, anti-inflammatory agents, calcium entry blockers, antineoplastic/antiproliferative/anti-mitotic compounds, anti-microbial compounds, anesthetic agents, nitric oxide donors, anti-coagulants, vascular cell growth promoting proteins, vascular cell growth protein inhibitors, vascular cell growth antibody inhibitors, cholesterol lowering drugs, vasodilating drugs, proteins that protects against cell death, cell cycle CDK protein inhibitors, anti-restenosis proteins, agents for treating malignancies, bone morphogenic proteins, and a polynucleotides encoding any of the above named proteins or protein inhibitors.

48. (Previously Presented) The medical device of claim 47 wherein the anti-thrombogenic protein is heparin, heparin derivatives, urokinase, or PPACK.

⁴⁰
49. (Currently Amended) The medical device of claim ³⁸47 wherein the antioxidant compounds is probucol or retinoic acid.

50. (Currently Amended) The method of claim 10 wherein the at least one of the one or more negatively charged -therapeutic agents is selected from the group consisting of: anti-thrombogenic proteins, antioxidant compounds, angiogenic proteins, agents which blocks smooth muscle cell proliferation, anti-inflammatory agents, calcium entry blockers, antineoplastic/antiproliferative/anti-mitotic compounds, anti-microbial compounds, anesthetic

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agents, nitric oxide donors, anti-coagulants, vascular cell growth promoting proteins, vascular cell growth protein inhibitors, vascular cell growth antibody inhibitors, cholesterol lowering drugs, vasodilating drugs, proteins that protects against cell death, cell cycle CDK protein inhibitors, anti-restenosis proteins, agents for treating malignancies, bone morphogenic proteins, and a polynucleotides encoding any of the above named proteins or protein inhibitors.

51. (Previously Presented) The method of claim 50 wherein the anti-thrombogenic protein is heparin, heparin derivatives, urokinase, or PPACK.

⁴³ 52. (Currently Amended) The method of claim ⁴¹50 wherein the antioxidant compounds is probucol or retinoic acid.

53. (Currently Amended) The medical device method of claim 19 wherein the at least one of the ~~one or more~~ negatively charged therapeutic agents is selected from the group consisting of: anti-thrombogenic proteins, antioxidant compounds, angiogenic proteins, agents which blocks smooth muscle cell proliferation, anti-inflammatory agents, calcium entry blockers, antineoplastic/antiproliferative/anti-mitotic compounds, anti-microbial compounds, anesthetic agents, nitric oxide donors, anti-coagulants, vascular cell growth promoting proteins, vascular cell growth protein inhibitors, vascular cell growth antibody inhibitors, cholesterol lowering drugs, vasodilating drugs, proteins that protects against cell death, cell cycle CDK protein inhibitors, anti-restenosis proteins, agents for treating malignancies, bone morphogenic proteins, and a polynucleotides encoding any of the above named proteins or protein inhibitors.

⁴⁵ 54. (Currently Amended) The medical device method of claim ⁴⁴53 wherein the anti-thrombogenic protein is heparin, heparin derivatives, urokinase, or PPACK.

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⁴⁶ 55. (Currently Amended) The medical device ⁴⁴method of claim ~~53~~ wherein the antioxidant compounds is probucol or retinoic acid.

56. (Currently Amended) The method of claim 28 wherein the at least one ~~of the one or more~~ negatively charged therapeutic agents is selected from the group consisting of: anti-thrombogenic proteins, antioxidant compounds, angiogenic proteins, agents which blocks smooth muscle cell proliferation, anti-inflammatory agents, calcium entry blockers, antineoplastic/antiproliferative/anti-mitotic compounds, anti-microbial compounds, anesthetic agents, nitric oxide donors, anti-coagulants, vascular cell growth promoting proteins, vascular cell growth protein inhibitors, vascular cell growth antibody inhibitors, cholesterol lowering drugs, vasodilating drugs, proteins that protects against cell death, cell cycle CDK protein inhibitors, anti-restenosis proteins, agents for treating malignancies, bone morphogenic proteins, and a polynucleotides encoding any of the above named proteins or protein inhibitors.

57. (Previously Presented) The method of claim 56 wherein the anti-thrombogenic protein is heparin, heparin derivatives, urokinase, or PPACK.

⁴⁹ 58. (Currently Amended) The method of claim ⁴⁷~~56~~ wherein the antioxidant compounds is probucol or retinoic acid.

59. (Currently Amended) The method of claim 38 wherein the at least one ~~of the one or more~~ negatively charged -therapeutic agents is selected from the group consisting of: anti-thrombogenic proteins, antioxidant compounds, angiogenic proteins, agents which blocks smooth muscle cell proliferation, anti-inflammatory agents, calcium entry blockers, antineoplastic/antiproliferative/anti-mitotic compounds, anti-microbial compounds, anesthetic agents, nitric oxide donors, anti-coagulants, vascular cell growth promoting proteins, vascular cell growth protein inhibitors, vascular cell growth antibody inhibitors, cholesterol lowering

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drugs, vasodilating drugs, proteins that protects against cell death, cell cycle CDK protein inhibitors, anti-restenosis proteins, agents for treating malignancies, bone morphogenic proteins, and a polynucleotides encoding any of the above named proteins or protein inhibitors.

60. (Previously Presented) The method of claim 59 wherein the anti-thrombogenic protein is heparin, heparin derivatives, urokinase, or PPACK.

⁵² 61. (Currently Amended) The method of claim ⁵⁰ 59 wherein the antioxidant compounds is probucol or retinoic acid.

62. (Currently Amended) A method of delivering a therapeutic agent to a mammal, the method comprising implanting a medical device at a desired location or tissue in a mammal, wherein the medical device is produced by a process comprising:

- (a) coating at least ~~a one~~ portion of ~~at least one surface of~~ the medical device with a cationic polyelectrolyte carrier to form a layer of cationic polyelectrolyte carrier;
- (b) washing the layer of cationic polyelectrolyte carrier with a washing solution;
- (c) adsorbing at least one ~~or more~~ negatively charged therapeutic agents onto the layer of cationic polyelectrolyte carrier to form a layer of at least one negatively charged therapeutic agent; and optionally
- (d) washing the layer of at least one negatively charged therapeutic agent with a washing solution and repeating steps (a) through (c) one or more times to form multiple layers of cationic polyelectrolyte carrier and at least one negatively charged therapeutic agent until a desired amount of at least one negatively charged therapeutic agent has been adsorbed onto the medical device.

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63. (Currently Amended) A method of delivering a polynucleotide DNA encoding a protein to a mammal, the method comprising implanting a medical device at a desired location or tissue in a mammal, wherein the medical device is prepared by:

- (i) coating at least ~~a~~one portion of ~~at least one surface of~~ the medical device with a cationic polyelectrolyte carrier to form a layer of cationic polyelectrolyte carrier;
- (ii) washing the layer of cationic polyelectrolyte carrier with a washing solution;
- (iii) adsorbing at least one ~~or more~~ negatively charged therapeutic agents onto the layer of cationic polyelectrolyte carrier to form a layer of at least one negatively charged therapeutic agent; and optionally
- (iv) washing the layer of at least one negatively charged therapeutic agent with a washing solution and repeating steps (i) through (iii) one or more times to form multiple layers of cationic polyelectrolyte carrier and at least one negatively charged therapeutic agent until a desired amount of the at least one negatively charged therapeutic agent has been adsorbed onto the medical device; wherein ~~the at least one of the one or more~~ negatively charged therapeutic agents is the polynucleotide DNA encoding a protein.

64. (Currently Amended) A method of delivering a DNA encoding a therapeutic protein to a mammal, the method comprising implanting a medical device at a desired location or tissue in a mammal, wherein the medical device is prepared by:

- (i) coating at least ~~a~~one portion of ~~at least one surface of~~ the medical device with a cationic polyelectrolyte carrier to form a layer of cationic polyelectrolyte carrier;
- (ii) washing the layer of cationic polyelectrolyte carrier with a washing solution;
- (iii) adsorbing at least one ~~one or more~~ negatively charged therapeutic agents onto the layer of cationic polyelectrolyte carrier to form a layer of at least one negatively charged therapeutic agent; and optionally
- (iv) washing the layer of at least one negatively charged therapeutic agent with a washing solution and repeating steps (i) through (iii) one or more times to form multiple layers of

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cationic polyelectrolyte carrier and at least one negatively charged therapeutic agent until a desired amount of at least one negatively charged therapeutic agent has been adsorbed onto the medical device; wherein the at least one of ~~the one or more~~ negatively charged therapeutic agents is a DNA encoding a therapeutic protein, wherein the therapeutic protein is selected from the group consisting of anti-thrombogenic proteins, angiogenic proteins, vascular cell growth promoting proteins, vascular cell growth protein inhibitors, proteins that protect against cell death, cell cycle CDK protein inhibitors, anti-restenosis proteins, and bone morphogenic proteins.

65. (Currently Amended) A method for inhibiting restenosis or the growth of tumor cells in a mammal, comprising:

(a) preparing a medical device by:

- (i) coating at least ~~a~~ portion of ~~at least one surface of~~ the medical device with a cationic polyelectrolyte carrier to form a layer of cationic polyelectrolyte carrier;
- (ii) washing the layer of cationic polyelectrolyte carrier with a washing solution;
- (iii) adsorbing at least one ~~or more~~ negatively charged therapeutic agents effective to inhibit restenosis or the growth of tumor cells onto the layer of cationic polyelectrolyte carrier to form a layer of at least one negatively charged therapeutic agent; and optionally
- (iv) washing the layer of negatively charged therapeutic agent with a washing solution and repeating steps (i) through (iii) one or more times to form multiple layers of cationic polyelectrolyte carrier and at least one negatively charged therapeutic agent until a desired amount of at least one negatively charged therapeutic agent has been adsorbed onto the medical device;

(b) implanting the medical device into a target location in a mammal;

wherein the at least one of ~~the one or more~~ negatively charged therapeutic agents is a DNA coding for an anti-proliferative protein.

66. (Currently Amended) A method for inducing the growth of blood vessels at a target location in a mammal, comprising:

(a) preparing a medical device by:

(i) coating at least ~~a~~ one portion of ~~at least one surface of~~ the medical device with a cationic polyelectrolyte carrier to form a layer of cationic polyelectrolyte carrier;

(ii) washing the layer of cationic polyelectrolyte carrier with a washing solution;

(iii) adsorbing at least one ~~one or more~~ negatively charged therapeutic agents effective to induce the growth of blood vessels onto the layer of cationic polyelectrolyte carrier to form a layer of at least one negatively charged therapeutic agent; and optionally

(iv) washing the layer of at least one negatively charged therapeutic agent with a washing solution and repeating steps (i) through (iii) one or more times to form multiple layers of cationic polyelectrolyte carrier and at least one negatively charged therapeutic agent until a desired amount of the least one negatively charged therapeutic agent has been adsorbed onto the medical device.

(b) implanting the medical device into the target location in a mammal;

wherein the ~~at least one of the one or more~~ negatively charged therapeutic agents is a DNA coding for an angiogenic protein.

67. (New) The medical device of claim 47, wherein the polynucleotide is inserted into an adenovirus vector.

68. (New) The method of claim 50, wherein the polynucleotide is inserted into an adenovirus vector.

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69. (New) The medical device of claim 53, wherein the polynucleotide is inserted into an adenovirus vector.

70. (New) The method of claim 56, wherein the polynucleotide is inserted into an adenovirus vector.